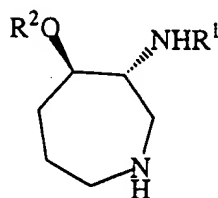


Claims

What is claimed is:

1. A process for the manufacture of compounds of the formula

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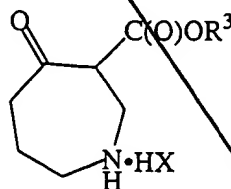


I

wherein R¹ and R² are independently an acyl residue of an aromatic carboxylic acid,

10 comprising:

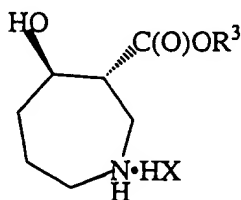
a) asymmetrically hydrogenating a compound of the formula



II,

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wherein R³ is lower-alkyl,
to a compound of the formula



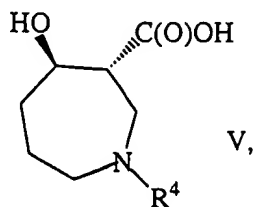
IV;

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b) providing a protecting group to the compound of formula IV;

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c) saponifying the compound of formula IV after step b), forming a compound of the formula

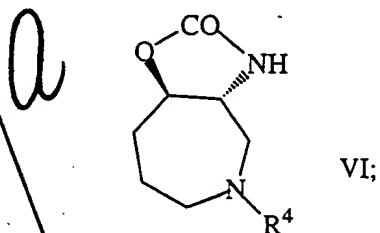


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wherein R^4 is a protecting group;

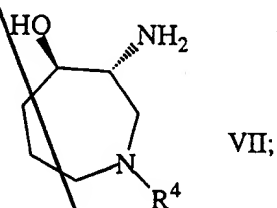
d) converting the compound of formula V into a compound of the formula

10



e) hydrolyzing the compound of formula VI into a compound of the formula

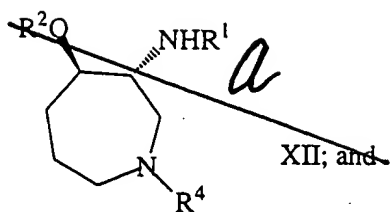
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f) N- and, respectively, O-acylating the compound of formula VII with an aromatic carboxylic acid of the formula $R^1\text{COOH}$ or $R^2\text{COOH}$ to form a compound of the formula

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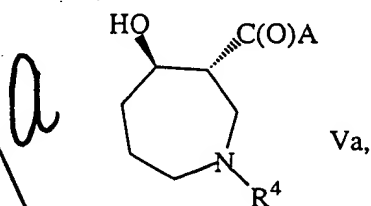


g) cleaving off protective groups on the compound of formula XII, to form the compound of formula I.

2. The process of claim 1, wherein R¹ and R² are p-hydroxybenzoyl.

3. The process of claim 1, further comprising in step c

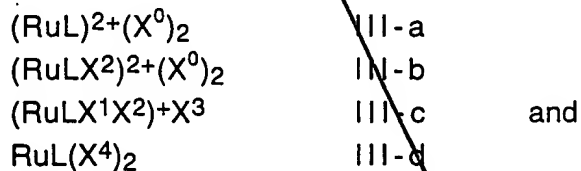
i) converting the compound of formula V into a compound of the formula



wherein A is azido or amino; and

ii) performing a Curtius or Hofmann degradation on the compound of formula Va to yield the compound of formula VI.

4. The process of claim 1, wherein the compound of formula II is hydrogenated in the presence of a rhodium-diphosphine complex catalyst having a formula selected from the formulae



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X⁻ is selected from the group consisting of BF₄⁻, ClO₄⁻, B(phenyl)₄⁻, SbF₆⁻, PF₆⁻ and Z¹-SO₃⁻;

X² is benzene, hexamethylbenzene or p-cymene;

X³ is selected from the group consisting of halide, ClO₄⁻, B(phenyl)₄⁻, SbF₆⁻, PF₆⁻, Z¹-SO₃⁻ and BF₄⁻;

X⁴ is selected from the group consisting of Z²-COO⁻, Z³-SO₃⁻, allyl and CH₃COCH=C(CH₃)O⁻;

10 Z¹ is halogenated lower alkyl or halogenated phenyl;

Z² is selected from the group consisting of lower alkyl, phenyl, halogenated lower alkyl and halogenated

15 Z^3 is lower alkyl or phenyl; and

L is an optically active atropiso-meric, diphosphine ligand.

5. The process of claim 4, wherein L is selected from the group consisting of

MeOBIPHEP (6,6'-Dimethoxybiphenyl-2,2'-diyl)bis-(diphenylphosphine);

BIPHEMP (6,6'-Dimethylbiphenyl-2,2'-diyl)bis-(diphenylphosphine);

25 BINAP [(1,1'-Binaphthyl)-2,2'-diyl]bis-(diphenylphosphine);

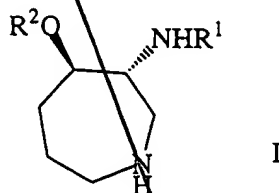
pTol-BIPHEMP (6,6'-Dimethylbiphenyl-2,2'-diyl)bis(di-(p-tolyl)phosphine);

30 pAn-MeOBIPHEP 6,6'-Dimethoxy-P,P',P',P'-tetrakis-(4-methoxy-phenyl)-biphenyl-2,2'-bis-phosphine;

pDMA-MeOBIPHEP 6,6'-Dimethoxy-P,P',P'-tetrakis-(4-dimethylamino-phenyl)-biphenyl-2,2'-bis-phosphine

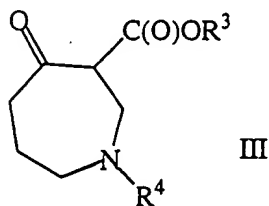
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25 7. A process for the manufacture of compounds of the formula



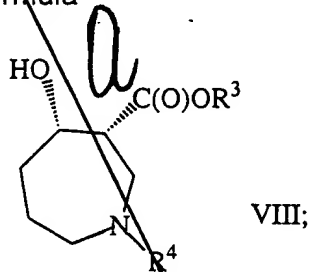
wherein R¹ and R² are independently an acyl residue of an aromatic carboxylic acid, comprising:

- a) microbially reducing a compound of the formula

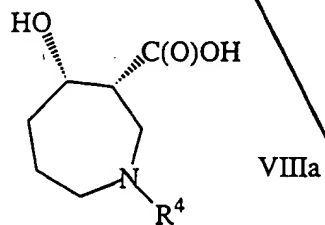


wherein R^3 is lower-alkyl and R^4 is a protecting group,

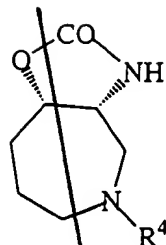
- 10 to a compound of the formula



- b) saponifying the compound of formula VIII to a compound of the
15 formula



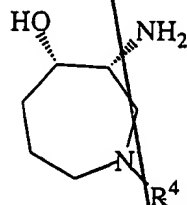
- c) transforming the compound of formula VIIIa into a compound of the formula



IX;

d) hydrolyzing the compound of formula IX into a compound of the formula

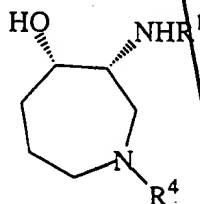
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X;

e) acylating the compound of formula X with an aromatic carboxylic acid of the formula R^1COOH to a compound of the formula

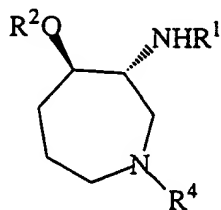
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XI;

f) acylating the compound of formula XI with an aromatic carboxylic acid or a reactive derivative thereof, to form a compound of the formula

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XII; and

g) cleaving off the protecting group R^4 from the compound of formula XII yielding the compound of formula I

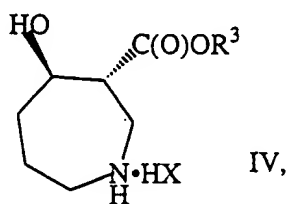
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8. The process of claim 7, wherein the compound of formula III is reduced using a culture of *Hanseniaspora uvarum* R 1052.

9. The process of claim 7, wherein R¹ and R² are p-hydroxybenzoyl.

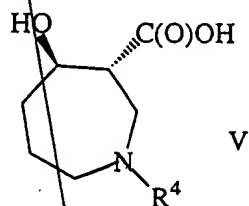
10. The compound of the formula



wherein R³ is lower alkyl.

11. The compound of claim 10, ethyl (3R,4R)-4-hydroxy-azepan-carboxylate hydrochloride.

12. The compound of the formula



wherein R⁴ is a protecting group.

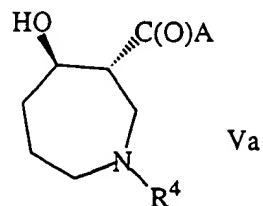
13. The compound of claim 12, (3R,4R)-4-Hydroxy-azepan-1,3-dicarboxylic acid 1-tert.-butyl ester.

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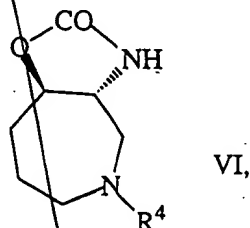
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14. ~~The~~ ^A compound of the formula



5 wherein A is azido or amino and R⁴ is a protecting group.

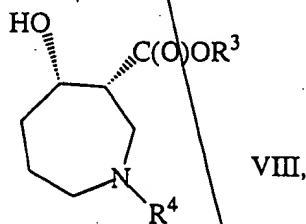
15. ~~The~~ ^A compound of the formula



10 wherein R⁴ is a protecting group.

16. The compound of claim 15, (3aR,8aR)-5-tert-Butoxycarbonyl-2-oxo-octahydro-oxazolo(4,b-c)azepine.

17. ~~The~~ ^A compound of the formula



20 wherein R³ is lower alkyl and R⁴ is a protecting group.

18. The compound of claim 17, ethyl (3R,4S)-1-(tert-butoxycarbonyl)-4-hydroxy-azepan-3-carboxylate.

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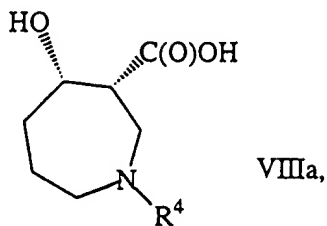
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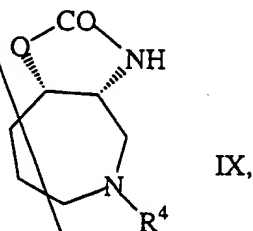
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20. The compound of claim 19, (3R,4S)-4-Hydroxy-azepan-1,3-dicarboxylic acid 1-tert-butyl ester.

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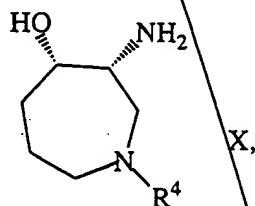


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wherein R^4 is a protecting group.

22. The compound of claim 21, tert-Butyl (3aR,8aS)-2-oxo-octahydro-oxazolo(4,b-c)azepine-5-carboxylate.

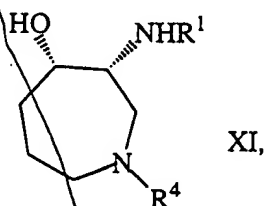
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wherein R^4 is a protecting group.

24. The compound of claim 23, tert-Butyl (3R,4S)-3-amino-4-hydroxy-azepan-1-carboxylate.

5 25. ~~The~~ compound of the formula



wherein R⁴ is a protecting group.

10 26. The compound of claim 25, tert-Butyl (3R,4S)-3-(4-tert-butoxy-benzoylamino)-4-hydroxy-azepan-1-carboxylate.

15 27. The compound tert-Butyl (3R,4R)-3-(4-tert-butoxy-benzoylamino)-4-(4-tert-butoxy-benzoyloxy)-azepan-1-carboxylate.

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